UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D. C. 20460

OFFICE OF
PREVENTION, PESTICIDES AND
TOXIC SUBSTANCES

December 6, 2001

MEMORANDUM

SUBJECT: Sodium Acifluorfen. (Chemical ID No. 114402, Case No. 2605). Dietary Exposure Analyses for the HED Preliminary Human Health Risk Assessment. No MRID #. DP Barcode No. D279173.

FROM: Felecia Fort, Chemist
Reregistration Branch I
Health Effects Division (7509C)

THRU: Whang Phang, Ph.D., Branch Senior Scientist
Reregistration Branch I
Health Effects Division (7509C)
and
Richard Griffin, Biologist
Dietary Exposure Science Advisory Council

TO: Kit Farwell, Veterinary Medical Officer
Reregistration Branch I
Health Effects Division (7509C)

BACKGROUND/ACTION REQUESTED

The Health Effects Division (HED) has revised the dietary risk analysis for the active ingredient, sodium acifluorfen (sodium 5-[2-chloro-4-(trifluoromethyl)-phenoxy]-2-nitrobenzoate) based on a change in the cancer Q_1*. A dietary analysis was previously completed on 5/23/00 (F. Fort, D266107) and 10/30/00 (F. Fort, D269130). **This revision reflects a change in the cancer dietary risk estimates only.** The supported (reassessed) tolerances include the following crops [40 CFR 180.383]: soybean (0.1 ppm), strawberry (0.05), peanut (0.1 ppm) and rice (0.2 ppm).

Executive Summary

Tier 1 and Tier 3 analyses were conducted. Tier 1 assessments were conducted using tolerance level residues and 100% crop treated (%CT) whereas the Tier 3 assessments included anticipated residues and % CT provided by the Biological and Economics Analysis Division (BEAD). Risk estimates above 10^{-6} are considered to be of concern. Residue inputs used in these analyses are shown in Table 2.

Using the revised Q_1* results in a maximum estimated lifetime cancer risk to the U.S. general population of 1.2 X 10^{-6} when a Tier 1 assessment was conducted and 5.2 X 10^{-8} when a Tier 3 assessment was performed. Based on the Tier 3 analysis, HED does not consider the cancer risk to be of concern (Table 3).

DETAILED CONSIDERATIONS

On January 13, 1988, the Cancer Peer Review Committee classified aciflourfen as a Group B2 - probable human carcinogen, and recommended that, for the purpose of risk characterization, a low dose extrapolation model be applied for quantification of human risk (Q_1^*). A Q_1* based upon male liver (carcinoma and/or adenoma) tumor rates was generated using mg/kg b.w.$^{\wedge 2/3}$'s/day cross species scaling factor (Aciflourfen, sodium salt (Tackle), Revised Quantitative Risk Assessment - 80 week B6C3F1 Mouse Dietary Study, B. Fisher, 8/25/93). A subsequent memo was generated to reflect the Agency policy change from use of the $^2/_3$'s to the $^3/_4$'s scaling factor in 1994 (REVISED Sodium Salt of Aciflourfen (Tackle™, Blazer™) Quantitative Risk Assessment (Q_1^*) Based On B6C3F1 Mouse Dietary Study Using mg/kg b.w.$^{\wedge 3/4}$'s/day Cross Species Scaling Factor, L. Brunsman, 8/23/2000, TXR No. 0014296). The Q_1* has again been revised to correct the mg/kg/day dose levels in light of the fact that the test material was originally believed to have been a 24% aqueous solution. Based on feed analysis data, it is now known to have been converted to pure sodium acifluorfen (Acifluorfen: Request of the Recalculation of the Q_1^*, P. Chin, 11/5/2001). The unit risk, Q_1^*(mg/kg/day)$^{-1}$, for Sodium Salt of Aciflourfen is 1.27 x $10^{-2.}$ [L. Brunsman, TXR No. 0050263,11/8/01]. The relevant doses and toxicological endpoints selected for dietary exposure scenarios are summarized in Table 1.

Table 1. Summary of Endpoints and Doses for Acifluorfen.

EXPOSURE SCENARIO	Population	DOSE (mg/kg/day)	RfD PAD(mg/kg/day)	ENDPOINT	STUDY
Acute Dietary	Female 13+ years old	NOEL=20 UF=100 FQPA SF = 10	aRfD = 0.2 aPAD = 0.02	Decreased fetal weight and increased incidences of dilated lateral ventricles of the brain	Developmental–rat
	General population	none	none	N/A	
Chronic Dietary	Female 13+ years old, Infants and Children	NOEL=1.25 UF=100 FQPA SF = 3	cRfD = 0.013 cPAD = 0.0043	based on kidney lesions, characterized predominantly by dilatation of tubules in the outer medulla, in females of both generations	2-generation reproduction–rat

	General populations	NOEL=1.25 UF=100 FQPA SF = 1	cRfD = 0.013 cPAD =0.013		
Cancer	US population	$Q_1^* = 1.27 \times 10^{-2}$**		classified it as a B2 carcinogen (probable human carcinogen)	Carcinogenicity - mice

**Revised from to 5.3×10^{-2} to 1.27×10^{-2}

Usage Information

BEAD provided information (F. Hernandez, 7/9/99) on the percent crop treated (%CT)[Attachment 3]. For the cancer analysis (Tier 3 only), the weighted average %CT was used and is entered as adjustment factor # 2 in the analyses. In all analyses 100% crop treated was used for strawberries because there is currently no registered use of this commodity.

Residue Data

Sodium acifluorfen is a contact herbicide currently registered for use on peanuts, rice, and soybeans. Tolerances for the combined residues of the herbicide sodium salt of acifluorfen, sodium 5-[2-chloro-4-(trifluoromethyl)phenoxy]-2-nitrobenzoic acid, and its metabolites (the corresponding acid, methyl ester, and amino analogues) have been established for rice, soybeans, and peanuts at 0.1 ppm; strawberries at 0.05 ppm and on meat, milk, and eggs at 0.02 ppm (40 CFR § 180.383). Although a tolerance for residues in/on strawberries exists, strawberries are currently not registered for use. IR-4, however, has stated that it will support this use; therefore, strawberries were included in this assessment (verbal communication between W. Hazel and H. Jamison, 5/15/00). The Metabolism Assessment Review Committee (MARC) determined that for livestock commodities, a Category 3 situation exists (no expectation of finite residues); livestock tolerances will therefore be revoked (W. Hazel, 5/5/00, D265602).

Anticipated residues were generated by J. Abbotts (12/7/92, D178405) and J. Garbus (8/29/94, D197871) and are based solely on field trial data. No monitoring data are available for sodium acifluorfen. Residues used in the analyses are shown in Table 2.

Processing Factors

Anticipated residues for peanut, soybean and rice processed products were determined based on processing studies submitted by the registrant. The data indicate that residues of acifluorfen and its metabolites do not concentrate in rice and peanut processed commodities and are reduced by 0.47X in soybean processed products (S. Knizner, D204306, 6/1/95 and D213553, 6/14/95). Residues used in the dietary risk analyses reflect the results of these studies; therefore, all DEEM default processing factors (Adjustment Factor #1) were changed to one.

Consumption Data

HED conducts dietary risk assessments using the Dietary Exposure Evaluation Model (DEEM™ Version 7.075), which incorporates consumption data generated in USDA's Continuing Surveys of Food Intakes by Individuals (CSFII), 1989-1992. For chronic dietary risk assessments, the three-day average of consumption for each sub-population is combined with average residues in commodities to determine average exposures in mg/kg/day.

Table 2. Summary of Anticipated Residues for Acifluorfen

Commodity	Data Used[1]	%Percent Crop Treated[2]	Reassessed Tolerance	Chronic Anticipated Residue, ppm[3]
Peanuts-butter	FT	11	0.1	0.006
Peanuts-hulled	FT	11	0.1	0.006
Peanuts-oil	FT	11	0.1	0.006
Rice - bran	FT	4	0.2	0.0025
Rice - milled	FT	4	0.2	0.0025
Rice - rough	FT	4	0.2	0.0025
Soybean-other	FT	9	0.1	0.005
Soybean-flour	FT	9	0.1	0.0024
Soybean -oil	FT	9	0.1	0.0024
Soybeans-protein isolate	FT	9	0.1	0.0024
Soybean-sprouted seed	FT	9	0.1	0.0024
Soybeans-flour	FT	9	0.1	0.0024
Strawberries[4]	FT	100	0.05	0.005
Strawberries - juice[4]	FT	100	0.05	0.005

1 FT = field trial data;

2 Percent Crop treated information was provided by BEAD (F. Hernandez, 7/9/99).

3. % CT not incorporated into chronic AR. % CT is entered as adjustment factor # 2 in the analyses.

4. Anticipated residue = ½ LOD

Conclusions

Tier 1 and Tier 3 analyses were conducted. Tier 1 assessments were conducted using tolerance level residues and 100% crop treated (%CT) whereas the Tier 3 assessments included anticipated residues and % CT provided by the Biological and Economics Analysis Division (BEAD).

Using the revised Q_1* results in a maximum estimated lifetime cancer risk to the U.S. general population of 1.2×10^{-6} when a Tier 1 assessment was conducted and 5.2×10^{-8} when a Tier 3 assessment was performed. Based on the Tier 3 analysis, HED does not consider the cancer risk to be of concern (Table 1). These assessments are considered to be somewhat conservative since they are based on field trial data.

Table 3. Summary of Acifluorfen Cancer Dietary Exposure and Risk Estimates.

Tier	Exposure	Lifetime Risk	
		Previous Assessment using a Q_1* of 5.3 x 10^{-2}	**Current Assessment using Q_1* of 1.2 x 10^{-2}**
Tier 1	0.000096	5.1 X 10^{-6}	**1.2 x 10^{-6}**
Tier 3	<0.000001	2.2 x 10^{-8}	**5.2 x 10^{-9}**

NOTE: The previous analyses show that the acute probabilistic dietary exposure and risk estimates are not of concern for the population subgroup considered, females 13-50 years old. The estimated exposure at the 95th percentile in the Tier 1 assessment is < 7% of the acute Population Adjusted Dose (aPAD). Incorporating anticipated residues and % CT (Tier 3) resulted in a % aPAD estimate of <1% at the 99.9th percentile of exposure. Likewise, chronic dietary exposure and risk were not of concern with less than 10% and less than 1% of the chronic Population Adjusted Dose (cPAD) consumed for all population subgroups in both the Tier 1 and Tier 3 analyses, respectively. Although the risk estimates at Tier 1 were below HED's concern, a Tier 3 was conducted to allow for an aggregate assessment which will include exposure from drinking water and acifluorfen residues from the application of the chemical, lactofen.

Table 4. Summary of Acifluorfen Chronic Dietary Exposure and Risk Estimates.[1]

Population Subgroup	**Chronic Assessment**			
	Tier 1[2]		**Tier 3[3]**	
	Exposure (mg/kg/day)	% cPAD	Exposure (mg/kg/day)	% cPAD
General US Population	0.000096	1	<0.000001	<1
All infants (<1 year)	0.000419	10	0.000001	<1
Children 1-6 years	0.000201	5	0.000001	<1
Children 7-12 years	0.000136	3	0.000001	<1
Females 13-50 years	0.00075	2	<0.000001	<1

1 The chronic PAD (cPAD) is 0.0043 for females 13+ years, infants and children; 0.013 mg/kg/day for U.S. Population and all other subgroups.

2 The Tier 1 assessment included tolerance level residues and 100% crop treated.

3 The Tier 3 assessment include anticipated residues and % CT information provided by BEAD.

Table 5. Summary of Acifluorfen Acute Dietary Exposure and Risk Estimates.[1]

Population Subgroup	**Acute Assessment**	
	Tier 1[2]	**Tier 3[3]**

	95th %-ile		99.9th %-ile	
	Exposure (mg/kg/day)	% aPAD	Exposure (mg/kg/day)	% aPAD
Females 13-50 years	0.000289	1	0.000024	<1

1 The acute Population Adjusted Dose (aPAD) is 0.02 for females 13+ years, no endpoint is established for the general population.
2 The Tier 1 assessment included tolerance level residues and 100% crop treated.
3 The Tier 3 assessment included anticipated residues and % CT information provided by BEAD.

cc: List B Rereg. File, Lashonia Richardson
RDI: WPhang / /01
7509C:FFort:RRB1:CM2:Rm 722H:703 305-7478:11/13/2001

Attachments

Attachment 1 Chronic and Cancer Dietary Assessment- Tier 1 (Tolerance Level and 100% CT)
Attachment 2 Chronic and Cancer Dietary Assessment- Tier 3 (Anticipated Residues and % CT)

Attachment 1 : Cancer Dietary Assessment- Tier 1 (Tolerance Level and 100% CT)

Residue File

```
U.S. Environmental Protection Agency                                  Ver. 7.73
DEEM Chronic analysis for ACIFLUORFEN                               1989-92 data
Residue file: C:\$MyFiles\Acifluorfen\Deemruns\tier1new qstar2.RS7
                                                                  Adjust. #2 used
Analysis Date 11-13-2001            Residue file dated: 11-13-2001/15:06:43/8
Q* = 0.0127
```

Food Code	Crop Grp	Food Name	RESIDUE (ppm)	Adj.Factors #1	#2	Comment
17	O	Strawberries	0.050000	1.000	1.000	
255	6A	Soybeans-sprouted seeds	0.100000	1.000	1.000	
270	15	Rice-rough (brown)	0.200000	1.000	1.000	
271	15	Rice-milled (white)	0.200000	1.000	1.000	
293	O	Peanuts-oil	0.100000	1.000	1.000	
297	6A	Soybeans-oil	0.100000	1.000	1.000	
303	6A	Soybean-other	0.100000	1.000	1.000	
304	6A	Soybeans-mature seeds dry	0.100000	1.000	1.000	
305	6A	Soybeans-flour (full fat)	0.100000	1.000	1.000	
306	6A	Soybeans-flour (low fat)	0.100000	1.000	1.000	
307	6A	Soybeans-flour (defatted)	0.100000	1.000	1.000	
403	O	Peanuts-butter	0.100000	1.000	1.000	
408	15	Rice-bran	0.200000	1.000	1.000	
416	O	Strawberries-juice	0.050000	1.000	1.000	
482	O	Soybeans-protein isolate	0.100000	1.000	1.000	
940	O	Peanuts-hulled	0.100000	1.000	1.000	

Results

```
U.S. Environmental Protection Agency                                  Ver. 7.73
DEEM Chronic analysis for ACIFLUORFEN                              (1989-92 data)
Residue file name: C:\$MyFiles\Acifluorfen\Deemruns\tier1new qstar2.RS7
                                                  Adjustment factor #2 used.
```

Analysis Date 11-13-2001/15:07:58 Residue file dated: 11-13-2001/15:06:43/8
Q* = 0.0127

Total exposure by population subgroup

Population Subgroup	Total Exposure mg/kg body wt/day	Total Exposure Lifetime risk (Q*= .0127)
U.S. Population (total)	0.000096	1.23E-06

Attachment 2 Cancer Dietary Assessment- Tier 3 (Anticipated Residues and % CT)

Residue File

```
U.S. Environmental Protection Agency                                    Ver. 7.73
DEEM Chronic analysis for ACIFLUORFEN                                 1989-92 data
Residue file: C:\$MyFiles\Acifluorfen\Deemruns\chronictier3 new qstar2.RS7
                                                                  Adjust. #2 used
Analysis Date 11-13-2001            Residue file dated: 11-13-2001/15:06:06/8
Q* = 0.0127
```

Food Code	Crop Grp	Food Name	RESIDUE (ppm)	Adj.Factors #1	#2	Comment
17	O	Strawberries	0.005000	1.000	1.000	
255	6A	Soybeans-sprouted seeds	0.002400	1.000	0.090	
270	15	Rice-rough (brown)	0.002500	1.000	0.040	
271	15	Rice-milled (white)	0.002500	1.000	0.040	
293	O	Peanuts-oil	0.006000	1.000	0.110	
297	6A	Soybeans-oil	0.002400	1.000	0.090	
303	6A	Soybean-other	0.005000	1.000	0.090	
304	6A	Soybeans-mature seeds dry	0.002400	1.000	0.090	
305	6A	Soybeans-flour (full fat)	0.002400	1.000	0.090	
306	6A	Soybeans-flour (low fat)	0.002400	1.000	0.090	
307	6A	Soybeans-flour (defatted)	0.002400	1.000	0.090	
403	O	Peanuts-butter	0.006000	1.000	0.110	
408	15	Rice-bran	0.002500	1.000	0.040	
416	O	Strawberries-juice	0.005000	1.000	1.000	
482	O	Soybeans-protein isolate	0.002400	1.000	0.090	
940	O	Peanuts-hulled	0.006000	1.000	0.110	

Results

```
U.S. Environmental Protection Agency                                    Ver. 7.73
DEEM Chronic analysis for ACIFLUORFEN                                (1989-92 data)
Residue file name: C:\$MyFiles\Acifluorfen\Deemruns\chronictier3 new qstar2.RS7
                                                    Adjustment factor #2 used.
Analysis Date 11-13-2001/15:07:23     Residue file dated: 11-13-2001/15:06:06/8
Q* = 0.0127
```

Total exposure by population subgroup

Population Subgroup	Total Exposure mg/kg body wt/day	Total Exposure Lifetime risk (Q*= .0127)
U.S. Population (total)	0.000000	5.19E-09

Attachment 3 **Quantitative Usage Analysis**

Quantitative Usage Analysis for Acifluorfen

Case Number: 2605 PC Code: 114402

Date: July 9, 1999 Analyst: Frank Hernandez

Based on available pesticide survey usage information for the years of 1987 through 1997, an annual estimate of acifluorfen total domestic usage averaged approximately one and a half million pounds active ingredient (a.i.) for over six million acres treated. Acifluorfen is a herbicide with its largest markets in terms of total pounds active ingredient allocated to soybeans (94%), peanuts (4%), rice (2%). Most of the usage is in AR, MS, IL, MO, IN, NC, VA, TX, and AL.

Site	Acres Grown (000)	Acres Treated (000)		% of Crop Treated		LB AI Applied (000)		Average Application Rate			States of Most Usage
		Wtd Avg	Est Max	Wtd Avg	Est Max	Wtd Avg	Est Max	lb ai/ acre /yr	#appl / yr	lb ai/ A/appl	(% of total lb ai used on this site)
Peanuts	1,610	180	307	11.19	19.04	56	113	0.3	1.2	0.3	NC GA VA TX AL MS 85%
Rice	2,921	119	183	4.07	6.27	28	48	0.2	1.1	0.2	AR MS MO 90%
Soybeans	62,879	5,771	7,257	9.18	11.54	1,360	1,710	0.2	1.1	0.2	AR MS IL MO MN IN 60%

Site	Acres Grown (000)	Acres Treated (000)		% of Crop Treated		LB AI Applied (000)		Average Application Rate			States of Most Usage
		Wtd Avg	Est Max	Wtd Avg	Est Max	Wtd Avg	Est Max	lb ai/ acre /yr	#appl / yr	lb ai/ A/appl	(% of total lb ai used on this site)
Total		6,070	6,908			1,444	1,657				

COLUMN HEADINGS

Wtd Avg = Weighted average--the most recent years and more reliable data are weighted more heavily.
Est Max = Estimated maximum, which is estimated from available data.
Average application rates are calculated from the weighted averages.

NOTES ON TABLE DATA

Usage data primarily covers 1987 - 1997. Calculations of the above numbers may not appear to agree because they are displayed as rounded to the nearest 1000 for acres treated or lb. a.i. (Therefore 0 = < 500)
to two decimal percentage points for % of crop treated.

SOURCES: EPA data, USDA, and National Center for Food and Agricultural Policy.